

## I CLAIM:

1. A method of treating a disease or condition mediated by increased phosphorylation comprising administering an effective amount of an extracellular phosphate-acceptor compound (EPAC) to an animal in need thereof.
- 5 2. The method of Claim 1 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.
3. The method of Claim 2 wherein the phosvitin is chicken phosvitin.
4. The method of Claim 2 wherein the phosvitin or fragment thereof is at least about 35% dephosphorylated.
- 10 5. The method of Claim 4 wherein the phosvitin or fragment thereof is at least about 50% dephosphorylated.
6. The method of Claim 5 wherein the phosvitin or fragment thereof is at least about 70% dephosphorylated.
7. The method of Claim 6 wherein the phosvitin or fragment thereof is at least 15 about 90% dephosphorylated.
8. The method of Claim 1 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.
- 16 9. The method of Claim 8 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of 20 the foregoing.
10. The method of Claim 9 wherein the casein is an  $\alpha_{S1}$ -casein or a fragment thereof.
11. The method of Claim 1 wherein the EPAC is an acylated albumin which is at least partially dephosphorylated.
- 25 12. The method of Claim 11 wherein the EPAC is an acetylated albumin which is at least partially dephosphorylated.
13. The method of Claim 1 wherein the EPAC is a peptide having the sequence:

$(Xaa_1)_m [Ac-Lys (Xaa_1)_n Xaa_2]_p (Xaa_1)_m$  or

(Xaa<sub>1</sub>)<sub>m</sub> [Ac-Lys (Xaa<sub>1</sub>)<sub>n</sub> Xaa<sub>2</sub> Xaa<sub>2</sub> (Xaa<sub>1</sub>)<sub>n</sub> Lys-Ac]<sub>p</sub> (Xaa<sub>1</sub>)<sub>m</sub>

wherein:

Ac is an acyl group;

Xaa<sub>1</sub> is any amino acid;

5 Xaa<sub>2</sub> is serine, threonine or tyrosine;

m is 0-10;

n is 1-3;

p is 1-5; and

10 m, n and p are selected so that the total number of amino acids is at least  
about twenty and/or each Xaa<sub>1</sub> is selected so that the peptide will be  
hydrophilic.

14. The method of Claim 13 wherein the peptide is Ac-Lys Cys Ala Ser [SEQ ID NO:1] or Ac-Lys Ala Ser Ser Ala Lys-Ac [SEQ ID NO:2].

15. The method of Claim 1 wherein the EPAC is a mixture of plasma proteins  
which are at least partially dephosphorylated.

16. The method of Claim 1 wherein the EPAC is a kinase substrate.

17. The method of Claim 16 wherein the kinase substrate is a casein kinase  
substrate having the sequence Arg Arg Lys Asp Leu His Asp Asp Glu Glu Asp Glu Ala  
Met Ser Ile Thr Ala [SEQ ID NO:3] or the sequence Arg Arg Arg Ala Asp Asp Ser Asp  
20 [SEQ ID NO:4].

18. The method of Claim 1 wherein the EPAC is a synthetic peptide comprising  
one or more phosphorylatable amino acids.

19. The method of Claim 18 wherein the synthetic peptide comprises one or more  
serines, threonines and/or tyrosines in a random sequence.

25 20. The method of Claim 18 wherein the synthetic peptide comprises one or more  
phosphorylation sites.

21. The method of Claim 1 wherein the EPAC is targeted to a selected cell, tissue  
or organ.

22. The method of any one of Claims 1-21 wherein the disease or condition is inflammation or an inflammatory disease or condition.
23. The method of any one of Claims 1-21 wherein the disease or condition is a skin disease or condition.
- 5 24. The method of Claim 23 wherein the skin disease or condition is inflammation or an inflammatory skin disease or condition.
25. The method of Claim 23 wherein the skin disease or condition is an allergic reaction.
26. The method of Claim 23 wherein the skin disease or condition is a burn.
- 10 27. The method of Claim 23 wherein the skin disease or condition is eczema or a dermatitis
28. The method of Claim 23 wherein the skin disease or condition is an acne.
29. The method of Claim 23 wherein the skin disease or condition is psoriasis.
30. The method of Claim 23 wherein the skin disease or condition is keratosis or
- 15 elastosis
31. The method of Claim 23 wherein the skin disease or condition is an infection.
32. The method of Claim 23 wherein the skin disease or condition is measles or chickenpox..
33. The method of any one of Claims 1-21 wherein the disease or condition is an
- 20 allergy, an autoimmune disease or another immune disorder.
34. The method of any one of Claims 1-21 wherein the disease or condition is a proliferative disorder.
35. The method of any one of Claims 1-21 wherein the disease or condition is an angiogenic disease or condition.
- 25 36. A method of treating cancer comprising administering an effective amount of a phosphate acceptor compound (PAC) to an animal in need thereof.
37. The method of Claim 36 wherein the PAC is an extracellular phosphate acceptor compound (EPAC).

38. The method of Claim 36 wherein the PAC is an intracellular phosphate acceptor compound (IPAC).

39. The method of Claim 38 wherein the IPAC is a peptide having the sequence:

(Xaa<sub>1</sub>)<sub>m</sub> [Ac-Lys (Xaa<sub>1</sub>)<sub>n</sub> Xaa<sub>2</sub>]<sub>p</sub> (Xaa<sub>1</sub>)<sub>m</sub> or

5 (Xaa<sub>1</sub>)<sub>m</sub> [Ac-Lys (Xaa<sub>1</sub>)<sub>n</sub> Xaa<sub>2</sub> Xaa<sub>2</sub> (Xaa<sub>1</sub>)<sub>n</sub> Lys-Ac]<sub>p</sub> (Xaa<sub>1</sub>)<sub>m</sub>

wherein:

Ac is an acyl group;

Xaa<sub>1</sub> is any amino acid;

Xaa<sub>2</sub> is serine, threonine or tyrosine;

10 m is 0-10;

n is 1-3;

p is 1-5; and

m, n and p are selected so that the total number of amino acids is less than about twenty and each Xaa<sub>1</sub> is selected so that the peptide will be  
15 hydrophobic.

40. The method of Claim 38 wherein the IPAC is a kinase substrate.

41. The method of Claim 38 wherein the IPAC is a synthetic peptide comprising one or more phosphorylatable amino acids.

20 42. The method of Claim 41 wherein the synthetic peptide comprises one or more serines, threonines and/or tyrosines in a random sequence.

43. The method of Claim 41 wherein the synthetic peptide comprises one or more phosphorylation sites.

44. The method of Claim 38 wherein the IPAC is targeted to cancer cells.

25 45. The method of any one of Claims 36-44 wherein the cancer is a carcinoma, a sarcoma, a brain cancer, a head cancer, a neck cancer, a breast cancer, a cervical cancer, an ovarian cancer, a uterine cancer, a prostate cancer, a stomach cancer, a colon cancer, a rectal cancer, a pancreatic cancer, a bladder cancer, a thyroid cancer, a hepatic cancer, a lung cancer, a bone cancer, a skin cancer, a blood cancer, a lymphoma or a leukemia.

46. A pharmaceutical composition comprising a phosphate acceptor compound (PAC) and a pharmaceutically-acceptable carrier.

47. The composition of Claim 46 wherein the PAC is an extracellular phosphate acceptor compound (EPAC).

5       48. The composition of Claim 47 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.

49. The composition of Claim 48 wherein the phosvitin is chicken phosvitin.

50. The composition of Claim 48 wherein the phosvitin or fragment thereof is at least about 35% dephosphorylated.

10      51. The composition of Claim 50 wherein the phosvitin or fragment thereof is at least about 50% dephosphorylated.

52. The composition of Claim 51 wherein the phosvitin or fragment thereof is at least about 70% dephosphorylated.

15      53. The composition of Claim 52 wherein the phosvitin or fragment thereof is at least about 90% dephosphorylated.

54. The composition of Claim 47 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.

20      55. The composition of Claim 54 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.

56. The composition of Claim 55 wherein the casein is an  $\alpha_{s1}$ -casein or a fragment thereof.

57. The composition of Claim 47 wherein the EPAC is an acylated albumin which is at least partially dephosphorylated.

25      58. The composition of Claim 57 wherein the EPAC is an acetylated albumin which is at least partially dephosphorylated.

59. The composition of Claim 47 wherein the EPAC is a peptide having the sequence:

(Xaa<sub>1</sub>)<sub>m</sub> [Ac-Lys (Xaa<sub>1</sub>)<sub>n</sub> Xaa<sub>2</sub>]<sub>p</sub> (Xaa<sub>1</sub>)<sub>m</sub> or  
(Xaa<sub>1</sub>)<sub>m</sub> [Ac-Lys (Xaa<sub>1</sub>)<sub>n</sub> Xaa<sub>2</sub> Xaa<sub>2</sub> (Xaa<sub>1</sub>)<sub>n</sub> Lys-Ac]<sub>p</sub> (Xaa<sub>1</sub>)<sub>m</sub>

wherein:

- 5            Ac is an acyl group;
- 10          Xaa<sub>1</sub> is any amino acid;
- Xaa<sub>2</sub> is serine, threonine or tyrosine;
- m is 0-10;
- n is 1-3;
- p is 1-5; and
- 10          m, n and p are selected so that the total number of amino acids is at least about twenty and/or each Xaa<sub>1</sub> is selected so that the peptide will be hydrophilic.

60. The composition of Claim 59 wherein the peptide is Ac-Lys Cys Ala Ser [SEQ ID NO:1] or Ac-Lys Ala Ser Ser Ala Lys-Ac [SEQ ID NO:2].

15          61. The composition of Claim 47 wherein the EPAC is a mixture of plasma proteins which are at least partially dephosphorylated.

62. The composition of Claim 47 wherein the EPAC is a kinase substrate.

15          63. The composition of Claim 62 wherein the kinase substrate is a casein kinase substrate having the sequence Arg Arg Lys Asp-Leu His Asp Asp Glu Glu Asp Glu Ala Met Ser Ile Thr Ala [SEQ ID NO:3] or the sequence Arg Arg Arg Ala Asp Asp Ser Asp [SEQ ID NO:4].

20          64. The composition of Claim 47 wherein the EPAC is a synthetic peptide comprising one or more phosphorylatable amino acids.

25          65. The composition of Claim 64 wherein the synthetic peptide comprises one or more serines, threonines and/or tyrosines in a random sequence.

66. The composition of Claim 64 wherein the synthetic peptide comprises one or more phosphorylation sites.

67. The composition of Claim 47 wherein the EPAC is attached to a targeting molecule.

68. The composition of any one of Claims 47-67 which is suitable for topical administration of the EPAC.

5       69. The composition of Claim 68 wherein the composition is suitable for topical administration of the EPAC to the skin of an animal.

70. The composition of Claim 69 wherein the composition is a cream, lotion, ointment, paste, gel, solution, spray or drops.

10     71. The composition of Claim 70 wherein the composition is a cream or ointment.

72. The composition of Claim 46 wherein the PAC is an intracellular phosphate acceptor compound (IPAC).

73. The composition of Claim 72 wherein the IPAC is a peptide having the sequence:

15        $(Xaa_1)_m [Ac-Lys (Xaa_1)_n Xaa_2]_p (Xaa_1)_m$  or

$(Xaa_1)_m [Ac-Lys (Xaa_1)_n Xaa_2 Xaa_2 (Xaa_1)_n Lys-Ac]_p (Xaa_1)_m$

wherein:

Ac is an acyl group;

Xaa<sub>1</sub> is any amino acid;

20       Xaa<sub>2</sub> is serine, threonine or tyrosine;

m is 0-10;

n is 1-3;

p is 1-5; and

25       m, n and p are selected so that the total number of amino acids is less than about twenty and each Xaa<sub>1</sub> is selected so that the peptide will be hydrophobic.

74. The composition of Claim 72 wherein the IPAC is a kinase substrate.

75. The composition of Claim 72 wherein the IPAC is a synthetic peptide comprising one or more phosphorylatable amino acids.

76. The composition of Claim 75 wherein the synthetic peptide comprises one or more serines, threonines and/or tyrosines in a random sequence.

5 77. The composition of Claim 75 wherein the synthetic peptide comprises one or more phosphorylation sites.

75. The composition of Claim 72 wherein the IPAC is attached to a targeting molecule.

10 76. A method for inhibiting increased phosphorylation in a cell, a tissue or an organ that has been removed from an animal comprising contacting the cell, tissue or organ with a solution or medium containing an effective amount of an extracellular phosphate acceptor compound (EPAC).

77. The method of Claim 76 wherein the EPAC inhibits inflammation.

15 78. The method of Claim 76 or 77 wherein the cell, tissue or organ is transplanted into an animal after being contacted with the solution or medium containing the EPAC.

79. A solution for contacting a tissue or an organ that has been removed from an animal comprising an extracellular phosphate acceptor compound (EPAC).

80. The solution of Claim 79 which comprises a combination of EPACs.

20 81. A kit for contacting a cell, a tissue or an organ that has been removed from an animal with an extracellular phosphate acceptor compound (EPAC) or a combination of EPACs, the kit comprising:

a container holding an EPAC;

a container holding a combination of EPACs; or

25 a plurality of containers each holding an EPAC, wherein each of the plurality of EPACs may be the same as, or different than, the other EPAC(s).

82. A method of inhibiting increased phosphorylation in a tissue of an animal's mouth comprising contacting the tissue with an effective amount of an extracellular phosphate acceptor compound (EPAC).

83. The method of Claim 82 wherein the tissue is treated prophylactically.
84. The method of Claim 83 wherein the tissue is treated as part of a prophylactic oral regimen.
85. The method of Claim 82 wherein the tissue is treated prior to surgery, during surgery, after surgery or combinations thereof.
86. The method of Claim 82 wherein the tissue is treated prior to a tooth extraction, during a tooth extraction, after a tooth extraction or combinations thereof.
87. The method of Claim 82 wherein all or substantially all of the tissues of the mouth are contacted with the EPAC.
88. A method of treating a disease or condition of a tissue of an animal's mouth that is mediated by increased phosphorylation, the method comprising contacting the tissue with an effective amount of an extracellular phosphate acceptor compound (EPAC).
89. The method of Claim 88 wherein all or substantially all of the tissues of the mouth are contacted with the EPAC.
90. A method of treating inflammation or an inflammatory disease or condition of a tissue of an animal's mouth comprising contacting the tissue with an effective amount of an extracellular phosphate acceptor compound (EPAC).
91. The method of Claim 90 wherein the inflammation is inflammation of the periodontal tissue.
92. The method of Claim 90 wherein the disease or condition is gingivitis.
93. The method of Claim 90 wherein the disease or condition is periodontitis.
94. The method of Claim 90 wherein the inflammation is associated with a surgery or a tooth extraction.
95. The method of Claim 90 wherein the disease or condition is a bacterial, yeast, fungal or viral infection.
96. The method of Claim 90 wherein the disease or condition is a canker sore, cold sore or ulcer.

97. The method of Claim 90 wherein all or substantially all of the tissues of the mouth are contacted with the EPAC..

98. A method of whitening one or more teeth of an animal comprising contacting a tissue of the animal's mouth with an effective amount of an extracellular phosphate acceptor compound (EPAC).

5        99. The method of Claim 98 wherein all or substantially all of the tissues of the mouth are contacted with the EPAC.

100. The method of Claim 98 wherein the tissue is contacted with the EPAC prior to whitening the teeth, during whitening of the teeth, after whitening the teeth, or  
10 combinations thereof.

101. The method of any one of Claims 82-100 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.

102. The method of Claim 101 wherein the phosvitin is chicken phosvitin.

15        103. The method of any one of Claims 82-100 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.

104. The method of Claim 103 wherein the casein is an  $\alpha_1$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.

105. The method of Claim 104 wherein the casein is  $\alpha_{S1}$ -casein.

20        106. An oral care product comprising an extracellular phosphate acceptor compound (EPAC).

107. The product of Claim 106 which is an oral care device.

108. The device of Claim 107 which is a suture or a dental floss.

109. The device of Claim 107 which is a strip.

25        110. The device of Claim 109 wherein the strip further comprises a tooth whitening agent.

111. The product of any one of Claims 106-110 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.

112. The product of Claim 111 wherein the phosvitin is chicken phosvitin.
113. The product of any one of Claims 106-110 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.
114. The product of Claim 113 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.
115. The product of Claim 114 wherein the casein is  $\alpha_{S1}$ -casein.
116. An oral care composition comprising an extracellular phosphate acceptor compound (EPAC) and a pharmaceutically-acceptable carrier.
117. The composition of Claim 116 wherein the composition is an ointment or a cream.
118. The composition of Claim 116 wherein the composition is a wash, a rinse, a gargle, a spray or a solution.
119. The composition of Claim 116 wherein the composition is a gel, a paste or a powder.
120. The composition of Claim 116 wherein the composition is a tablet, a gum, a lozenge, a mint, a film or a patch.
121. The composition of Claim 116 wherein the composition is a tooth whitening composition.
122. The composition of any one of Claims 116-121 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.
123. The composition of Claim 122 wherein the phosvitin is chicken phosvitin.
124. The composition of any one of Claims 116-121 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.
125. The composition of Claim 124 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.
126. The composition of Claim 125 wherein the casein is  $\alpha_{S1}$ -casein.

127. A kit comprising an oral care product, the oral care product comprising an extracellular phosphate acceptor compound (EPAC).

128. A kit comprising an oral care device, the oral care device comprising an extracellular phosphate acceptor compound (EPAC).

5 129. The kit of Claim 128 wherein the device is a strip.

130. The kit of Claim 129 wherein the strip further comprises a tooth whitening agent.

131. The kit of Claim 128 wherein the kit further comprises a tooth whitening composition.

10 132. A kit comprising an oral care composition, the oral care composition comprising an extracellular phosphate acceptor compound (EPAC) and a pharmaceutically-acceptable carrier.

133. The kit of Claim 132 wherein the kit further comprises a tooth whitening composition.

15 134. The kit of Claim 132 wherein the kit further comprises a strip comprising a tooth whitening agent.

135. The kit of any one of Claims 127-134 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.

136. The kit of Claim 135 wherein the phosvitin is chicken phosvitin.

20 137. The kit of any one of Claims 127-134 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.

138. The kit of Claim 137 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.

25 139. The kit of Claim 138 wherein the casein is  $\alpha_{S1}$ -casein.

140. A method of inhibiting increased phosphorylation in an animal's skin comprising contacting the skin with an effective amount of an extracellular phosphate acceptor compound (EPAC).

141. The method of Claim 140 wherein the skin is treated prophylactially.
142. A personal care product comprising an extracellular phosphate acceptor compound (EPAC).
  143. The product of Claim 142 which is a personal care device.
    - 5 144. The device of Claim 143 which is a sponge, a cloth, a wipe or a pad.
    145. The device of Claim 143 which is a bandage, a suture or a surgical sponge.
    146. The device of Claim 143 which is a swab.
  147. The product of any one of Claims 142-146 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.
    - 10 148. The product of Claim 147 wherein the phosvitin is chicken phosvitin.
    149. The product of any one of Claims 142-146 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.
  150. The product of Claim 149 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.
    - 15 151. The product of Claim 150 wherein the casein is  $\alpha_{S1}$ -casein.
    152. A personal care composition comprising an extracellular phosphate acceptor compound (EPAC) and a pharmaceutically-acceptable carrier.
  153. The composition of Claim 152 wherein the composition is a cream or a lotion.
    - 20 154. The composition of Claim 153 wherein the composition is a suntan cream or lotion.
    155. The composition of Claim 153 wherein the composition is a moisturizing cream or lotion.
  156. The composition of Claim 152 wherein the composition is a wash, a rinse or a solution.
    - 25 157. The composition of Claim 152 wherein the composition is a gel or an ointment.

158. The composition of Claim 152 wherein the composition is a powder.
159. The composition of Claim 152 wherein the composition is a lipstick, lip gloss or lip balm.
160. The composition of any one of Claims 152-159 wherein the EPAC is a phosphovitin or a fragment thereof which is at least partially dephosphorylated.  
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161. The composition of Claim 160 wherein the phosphovitin is chicken phosphovitin.
162. The composition of any one of Claims 152-159 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.
163. The composition of Claim 162 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein,  
10 a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.
164. The composition of Claim 163 wherein the casein is  $\alpha_{S1}$ -casein.
165. A kit comprising a personal care product, the personal care product comprising an extracellular phosphate acceptor compound (EPAC).
166. A kit comprising a personal care device, the personal care device comprising  
15 an extracellular phosphate acceptor compound (EPAC).
167. The kit of Claim 166 wherein the device is a sponge, a cloth, a wipe or a pad.
168. The kit of Claim 166 wherein the device is a bandage, a suture or a surgical  
20 sponge.
169. The kit of Claim 166 wherein the device is a swab.
170. A kit comprising a personal care composition, the personal care composition comprising an extracellular phosphate acceptor compound (EPAC) and a pharmaceutically-acceptable topical carrier.
171. The kit of Claim 170 wherein the composition is a cream or a lotion.  
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172. The kit of Claim 171 wherein the composition is a suntan cream or lotion.
173. The kit of Claim 171 wherein the composition is a moisturizing cream or lotion.

174. The kit of Claim 170 wherein the composition is a wash, a rinse or a solution.

175. The kit of Claim 170 wherein the composition is a gel or an ointment.

176. The kit of Claim 170 wherein the composition is a powder.

5 177. The kit of Claim 170 wherein the composition is a lipstick, lip gloss or lip balm.

178. The kit of any one of Claims 165-177 wherein the EPAC is a phosvitin or a fragment thereof which is at least partially dephosphorylated.

179. The kit of Claim 178 wherein the phosvitin is chicken phosvitin.

10 180. The kit of any one of Claims 165-177 wherein the EPAC is a casein or a fragment thereof which is at least partially dephosphorylated.

181. The kit of Claim 180 wherein the casein is an  $\alpha$ -casein, a  $\beta$ -casein, a  $\gamma$ -casein, a  $\kappa$ -casein, a fragment of one of the foregoing, or a combination of one or more of the foregoing.

15 182. The kit of Claim 181 wherein the casein is  $\alpha_{S1}$ -casein.